Remarks

Claims 27-29, 32, 35 and 38 have been amended, claim 31 has been cancelled, new claims 39-45 have been added, and therefore claims 27-30 and 32-45 are pending in this application. In view of the above-amendments and the following remarks, it is respectfully submitted that these claims are allowable.

The Examiner has indicated at paragraph 4 of the Action that the instant inventorship has been assumed to include two inventors. However, Applicant submitted on August 3, 1999 a Petition Deleting Correctly Named Original Person Who Is Not An Inventor Of Invention Now Being Claimed under 37 CFR 1.48(b). Applicants resubmitted a copy of this Petition with the Amendment dated August 14, 2000. If the Examiner requires another copy of this Petition, the undersigned will be pleased to do so at the Examiner's request. Accordingly, Edward L. Carver, Jr. is the sole inventor of the claims currently pending in this application and it is believed that this issue has been obviated.

Claims 27-35 and 38 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Yamamoto in view of Kabata, Taylor, Dixon, Halliday or Robertson and Callan or Weiser. Alternatively, claims 27-35 and 38 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Cellect Hematology in view of Kabata, Taylor, Dixon, Halliday, Robertson and Callan or Weiser (JAVMA 1987). The Examiner's grounds for rejection are hereinafter traversed, and reconsideration is respectfully requested.

It is respectfully submitted that none of the cited references teach or suggest adjusting the volumetric ratio of lysing agent to blood in correspondence with an operator input indicative of the species of the blood as defined in each of independent claims 27, 35, and 38, and new independent claim 40.

As has been established, Yamamoto shows an automatic blood analyzer but fails to teach or suggest an apparatus comprising a control unit or like means for adjusting the volumetric ratio of lysing agent to blood in correspondence with an operator input indicative of the species of the blood. Rather, as recognized by the Examiner, Yamamoto discloses a system that is fixed to make the same dilution ratios, with the same volumes of reagent-mixture components for every blood sample.

Kabata likewise does not teach or suggest adjusting or modifying the volumetric ratio of lysing agent to blood to correspond to an operator input and species, as recited in independent claims 27, 35, 38 and 40. Kabata's suggestion to adapt the commercially-available software for human blood so that it may be better used for research purposes in connection with animal blood concerns changing the histogram thresholds to accommodate animal (rabbit), as opposed to human cell types. The thresholds divide the cell populations on the histograms, and they cannot be changed on the systems identified (see, for example, Figure 2 of Kabata showing the thresholds in solid lines). Accordingly, Kabata suggests that the software might be adapted for research purposes to adjust the histogram thresholds to better accommodate the animal cell types tested. The "Technicon H1" software identified by Kabata similarly modified the histogram thresholds for rats and dogs, but did not require different reagent mixtures for the different species. Accordingly, Kabata makes no teaching or suggestion of adjusting or creating different reagent mixtures in response to different operator inputs, much less adjusting the volumetric ratio of lysing agent to blood to correspond to any one of a plurality of different operator inputs and respective species, as recited in independent claims 27, 35, 38 and 40. Thus, Kabata does not teach or suggest modification of Yamamoto to achieve the claimed invention.

Taylor discusses various staining techniques for flow cytometry, but does not suggest adjusting or creating different reagent mixtures. Accordingly, Taylor does not materially add to the teachings of Yamamoto and Kabata with respect to the present invention.

Callen is not prior art with respect to the present invention. Callen was published in October 1992, less than one year prior to the effective filing date of the present application

(January 21, 1993). In any event, and without admitting that Callen is prior art with respect to the present invention, Callen shows evaluation of a system for hemoglobin measurement in dogs, cats, horses, and cows. Although Callen summarizes test result range differentials between those species, Callen does not suggest alteration of the testing process for different species. Thus, Callen does not teach or suggest changing the ratio of lysing agent to blood for different species, but rather effectively teaches away from doing so by showing acceptable results obtained without regard to species during the actual testing. Therefore, even if Callen were prior art with respect to the present invention, which it is not, it would not materially add to the teachings of Yamamoto, Kabata, and Taylor with respect to the present invention.

Weiser discusses various hematological techniques for different species, but does not suggest adjusting or creating different reagent mixtures. Weiser shows alteration of a device aperture current in order to count particles of sizes specific to common veterinary subjects. Weiser also shows doubling the dilution ratio where the particles are too numerous to be counted accurately by the subject device. Weiser does not make any suggestion to adjust the volumetric ratio of lysing agent to blood according to the subject species. Accordingly, Weiser does not materially add to the teachings of Yamamoto, Kabata, Taylor, and Callen with respect to the present invention.

Dixon shows experimental results derived from tests using non-standard concentrations of the lysing agent Zapoglobin on canine leukocytes. In sum, Dixon concludes that adjusting the volume of the lytic agent has no significant effect, but rather increasing the time of exposure to the standard concentration of the lytic agent did significantly increase lysis. Specifically, Dixon states in the abstract on page 249: "Canine leukocytes did not show significantly increased lysis when subjected to Zapoglobin at approximately four times the standard concentration, but did do so on exposure to the standard concentration for longer than five minutes". See also FIG. 2 on page 251 where the effect of high and low concentrations of Zapoglobin on leukocyte counts are compared reflecting virtually no difference.

Accordingly, Dixon specifically teaches that changing the standard concentration of lytic agent has no significant effect on increasing lysis, and therefore Dixon, in effect, teaches away from adjusting the volume of lyse to blood in response to different operator inputs indicative of different species, as recited in the independent claims. Rather, if anything, Dixon might suggest that one could change the exposure time to the standard concentration of the lytic agent in order to increase or decrease lysis. The paragraph cited by the Examiner at page 252 of Dixon similarly in no way teaches or suggests the present invention as recited in the independent claims. Rather, this paragraph merely reiterates the conclusions set forth in the abstract on page 249.

The non-obvious nature of the present invention over Dixon is further evidenced by the more than 10 year period between the publishing of the Dixon reference and the filing of the present application. Although Dixon taught that there was no concentration dependent effect for the Zapoglobin lysing agent on canine leukocytes, a commercial embodiment of the present invention does accurately analyze canine leukocytes via automatic adjustment of lysing agent mixtures upon the pressing of a button corresponding to the canine species, in spite of the contrary teachings of Dixon. Thus, it would not have been obvious for one of average skill in the pertinent art to apply the teachings of Dixon in order to derive the present invention.

Lastly, the newly cited references of Halliday et al. and Robertson et al. do not materially add to the teachings of the other cited references with respect to the presently claimed invention. Halliday et al. do not teach or suggest in any way adjusting the ratio of lyse to blood on a species-by-species basis, as recited in the amended and new independent claims. Rather, Halliday et al. teach using the same ratio as prescribed by the "standard Coulter Counter technique". The only difference to the standard Coulter Counter technique suggested by Halliday et al. was to change the order in which the components were mixed. (See Halliday et al. at 354).

The Examiner points out that Halliday et al. state at the end of the paper that similar variations have been found in "isolated specimens" of sheep and cat blood. However, this does not in any way teach or suggest the claimed invention. Rather, Halliday et al. make no teaching or suggestion as to what the cause of this variation might be. Further, Halliday et al.'s statement that the variation occurred only in "isolated specimens" would reasonably lead one of ordinary skill in the pertinent art to simply believe that the standard Coulter Counter technique is acceptable for most sheep and cats. Again, Halliday et al. make no teaching or suggestion of adjusting the volumetric ratio of lyse to blood on a species-by-species basis as recited in the present claims.

Robertson et al. do not relate in any way to automated hematology analyzers, much less such analyzers that adjust the ratio of lyse to blood on a species-by-species basis, as recited in the present claims. Rather, Robertson et al.'s paper is directed solely to modified staining techniques for avian blood cells. Although the Examiner correctly points out that Robertson et al. mention the prior development of a diluent then used widely by avian hematologists, there is no description of the diluent, much less any teaching or suggestion of modifying the lyse/diluent ratio, as suggested by the Examiner.

In sum, Halliday et al. and Robinson et al. do not in any reasonably clear or precise way show that there is a species dependent response to the ratio of lyse to blood, much less teach or suggest modifying any of the other references of record to create analyzers that adjust the ratio of lyse to blood on a species-by-species basis, as recited in independent claims 27, 35, 38 and 40.

Accordingly, it is respectfully submitted that independent claims 27, 35, 38 and 40 are unobvious over the cited references for at least these reasons. It is further submitted that the

dependent claims are likewise unobvious over the cited references for at least the same reasons as the independent claims, and for reciting additional patentable subject matter.

It is therefore respectfully submitted that claims 27-30 and 32-45 are allowable. All issues raised by the Examiner having been addressed, an early action to that effect is earnestly solicited.

The Examiner is hereby authorized to charge our Deposit Account No. 50-1631 in the amount of $40.00 for the fee for the extra independent claim. No additional fee is believed to be required; however, if an additional fee is required, or otherwise if necessary to cover any deficiency in fees already paid, authorization is hereby given to charge our Deposit Account No. 50-1631.

If the Examiner has any questions or comments in connection with any of the issues herein, or otherwise if it would facilitate the examination of this application, the Examiner is respectfully urged to call the undersigned at the telephone number below.

Respectfully submitted,

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VERSION OF AMENDED CLAIMS WITH MARKINGS TO SHOW THE CHANGES MADE

27. (Amended Four Times) A method for making a plurality of different reagent mixtures comprising blood and analyzing particle distributions of the reagent mixtures, wherein each reagent mixture corresponds to a respective operator input indicative of a respective species of blood, and the method is performed with an apparatus having at least one pump, at least one reagent chamber containing at least one lysing agent, a sensing unit defining a counting orifice for receiving a reagent mixture and analyzing a particle distribution of the reagent mixture, and a control unit responsive to each operator input to control the at least one pump to make a respective reagent mixture having a volumetric ratio of the at least one lysing agent to blood corresponding to the respective operator input and species of blood, and to further control the sensing unit to analyze a particle distribution of the reagent mixture, the method comprising the following steps:

adjusting the volumetric ratio of the at least one lysing agent to blood, in response to an operator input indicative of a respective species of blood, to correspond to the respective operator input, and thereby form a predetermined reagent mixture corresponding to the respective operator input and species of blood, said adjusting including:

selecting at least one lysing agent corresponding to the respective operator input;

pumping with the at least one pump a predetermined volume of the at least one lysing agent corresponding to the respective operator input;

pumping with the at least one pump a predetermined volume of [at least one other reagent-mixture component comprising] blood [and] corresponding to the respective operator input;

intermixing the predetermined volumes of the at least one lysing agent and [the at least one other reagent-mixture component comprising] blood, and in turn creating the predetermined reagent mixture corresponding to the respective operator input; and

introducing the predetermined reagent mixture through the counting orifice of the sensing unit and sensing a particle distribution of said reagent mixture.

28. (Amended) A method as defined in claim 27, [wherein the reagent-mixture components of a plurality of the different reagent mixtures include (i) blood and (ii) at least one lysing agent, and the method comprises] <u>further comprising</u> the steps of:

in response to each of a plurality of different operator inputs, selecting the ratio of blood to the at least one lysing agent in the corresponding reagent mixture;

pumping with the at least one pump a predetermined volume of the at least one selected lysing agent corresponding to the respective blood/lysing agent ratio;

pumping with the at least one pump a predetermined volume of blood corresponding to the respective blood/lysing agent ratio; and

intermixing the predetermined volumes of blood and the least one lysing agent, and in turn creating a reagent mixture corresponding to the respective operator input.

29. (Amended) A method as defined in claim 28, further comprising the steps of:

in response to each of a plurality of operator inputs, selecting the ratio of blood to at least one first lysing agent and at least one second lysing agent in the respective reagent mixture;

pumping with the at least one pump a predetermined volume of the at least one first lysing agent corresponding to the respective blood/lysing agent ratio;

pumping with the at least one pump a predetermined volume of the at least one second lysing agent corresponding to the respective blood/lysing agent ratio;

pumping with the at least one pump a predetermined volume of blood corresponding to the respective blood/lysing agent ratio; and

intermixing the predetermined volumes of blood and the first and second lysing agents, and in turn creating a reagent mixture corresponding to the respective operator input.

32. (Amended) A method as defined in claim 30, wherein the [at least one other] reagent-mixture components include[s] (i) a predetermined volume of blood, and (ii) a predetermined volume of diluent.

35. (Amended Thrice) An apparatus for making a plurality of reagent mixtures comprising blood and analyzing particle distributions of the reagent mixtures, comprising:

at least one pump;

at least one reagent chamber coupled in fluid communication with the at least one pump and containing at least one lysing agent;

a sensing unit defining a counting orifice for receiving a reagent mixture and analyzing a particle distribution of the reagent mixture; and

means for adjusting the volumetric ratio of blood to the at least one lysing agent for creating a plurality of different reagent mixtures, each corresponding to a [different] respective operator input indicative of [a] at least one respective species of blood, and for controlling the at least one pump in response to each operator input to pump predetermined volumes of blood and the at least one lysing agent in accordance with the blood/lysing agent ratio corresponding to the respective operator input and species of blood, said means further controlling the at least one pump to

(i) intermix the predetermined volumes of blood and the at least one lysing agent and thereby create the reagent mixture corresponding to the respective operator input, and

(ii) introduce the reagent mixture through the counting orifice of the sensing unit for sensing a particle distribution of the reagent mixture.

38. (Amended Twice) An apparatus for making a plurality of reagent mixtures for multi-species hematology testing, and for sensing particle distributions of the mixtures for multi-species hematology analysis, comprising:

at least one reagent chamber for containing at least one lysing agent;

at least one pump coupled in fluid communication with the at least one reagent chamber;

[at least one valve coupled in fluid communication with the at least one pump for introducing a blood specimen corresponding to any one of a plurality of species;

a control unit electrically coupled to the at least one pump for adjusting the volumetric ratio of the blood specimen to the at least one lysing agent in correspondence with an operator input corresponding to a respective one of the plurality of species;]

a mixing chamber coupled in fluid communication with the at least one pump for receiving [the pumped volumes of the respective blood specimen and] the at least one lysing agent and a predetermined volume of a blood specimen corresponding to any one of a plurality of different species [creating a reagent mixture therefrom having a blood to lysing agent volumetric ratio corresponding to the operator input and respective species to thereby create a plurality of different reagent mixtures having a plurality of blood to lysing agent volumetric ratios corresponding to a plurality of different operator inputs and respective species];

a control unit electrically coupled to the at least one pump for adjusting the volumetric ratio of the blood specimen to the at least one lysing agent in correspondence with an operator input corresponding to a respective one of the plurality of species and, in turn, creating a reagent mixture therefrom having a blood to lysing agent volumetric ratio corresponding to the operator input and respective species; and

a sensing unit coupled in fluid communication with the at least one pump and defining at least one counting orifice for receiving a reagent mixture and analyzing a particle distribution of the reagent mixture.